

Applicants request a three-month extension of time to file this reply and
enclose a check for the requisite fee in payment of the extension fees pursuant to
37 C.F.R. § 1.17(a)(3).

Please amend the application as follows:

IN THE SPECIFICATION:

On page 16, line 17, after "ECACC" and before "as Accession numbers" please
insert European Collection of Cell Cultures, CAMR (Center for Applied Microbiology
and Research), Salisbury, Wiltshire, SP4 OJG, England,

IN THE CLAIMS:

Please cancel claims 2, 5, 10-12 and 14.

Please amend claims 1, 3-4, 6-8, 13, and 15-24 as follows:

1. (Amended) A cell line [derived] obtained from a transgenic
[mammal] rat comprising:
- (i) a conditional oncogene, transforming gene or immortalizing gene or
a cell cycle affecting gene[; and] operably linked to
 - (ii) a cell type specific promoter.
3. (Amended) A cell line as claimed in claim 1 which is a neuronal
cell line[, mammary cell line, liver cell line or kidney cell line].

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4. (Amended) A cell line as claimed in claim 3 in which the [cell line is a neuronal cell line and the] cell type specific promoter is a human NF-L gene promoter.

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6. (Amended) A cell line as claimed in any of [the preceding claims] claims 1, 3, or 4 in which the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is a SV40tsA58 gene.

7. (Amended) A cell line as claimed in any of claims 1 [to 5] , 3, or 4 in which the conditional oncogene, transforming gene, immortalising gene or the cell cycle affecting gene is a C Erb $\beta 2$ gene or a TGF α gene.

8. (Amended) A cell line as claimed in claim 1 in which the conditional oncogene, transforming gene or the cell cycle affecting gene or immortalizing gene is a SV40tsA58 gene and the cell type specific promoter is a human NF-L gene promoter.

13. (Amended) A method [for] of producing a transgenic [mammal,] rat, comprising:

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(i) causing a female [mammal] rat to super-ovulate by supplying her with a regular supply of Follicle Stimulating Hormone (FSH) prior to mating;

(ii) mating or artificially inseminating the female [mammal] rat;

(iii) obtaining the resulting embryo from the female [mammal] rat; and

(iv) incorporating

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CONT.

- (i) a conditional oncogene, transforming gene or immortalising gene or a cell cycle affecting gene[; and] operably linked to
- (ii) a cell specific promoter into the genome of the [mammalian] rat embryo.

15. (Amended) A method a[n]s claimed in claim [14] 13 wherein the FSH is supplied continuously.

16. (Amended) A method as claimed in claims [14] 13 or 15 wherein the supply of FSH is from 2mg to 8mg and the FSH is supplied over a 1 to 4 day period.

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17. (Amended) A transgenic [mammal] rat whose germ cells and somatic cells contain
- (i) a conditional oncogene, transforming gene or immortalising gene or a cell cycle affecting gene[; and] operably linked to
 - (ii) a cell type specific promoter as a result of chromosomal incorporation into the [mammalian] rat genome or into the genome of an ancestor of said [mammal] rat.

18. (Amended) A transgenic [mammal] rat as claimed in claim 17, wherein the [mammal is a rat and the] conditional oncogene, transforming gene, immortalising gene, or the cell cycle affecting gene is a C Erb β 2 gene or a TGF α gene or a SV40tsA58 gene.

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19. (Amended) A method of testing a material suspected of being a carcinogen, said method comprising [exposing a mammal produced according to a method of the invention] subjecting a rat according to claim 17 or 18 or a rat produced according to the method of any of claims 13 or 15 or an ancestor thereof or cells or tissue from a cell line of [the invention] any of claims 1, 3, 4, 6, 7, 8, or 9, to said material and detecting neoplasms as an indication of carcinogenicity.

20. (Amended) A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising [treating] administering said material to a [mammal produced according to a method of the invention] rat according to claim 17 or 18 or a rat produced according to a method of claims 13 or 15 or an ancestor thereof or cells or tissues from a cell line of [the invention] any of claims 1, 3, 4, 6, 7, 8, or 9, [with said material] and detecting a reduced incidence of development or neoplasms, compared to an untreated [mammal] rat, as an indication of said protection.

21. (Amended) A method of [providing] obtaining a cell line comprising culturing a somatic cell obtained from a transgenic [mammal] rat as claimed in claim 17 or 18 or an ancestor thereof [according to the invention].

22. (Amended) A cell derived for a cell line obtained from a transgenic [mammal] rat as claimed in claim 17 or 18 or ancestor thereof [according to the invention].

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23. (Amended) A method of [providing] obtaining a transgenic tissue comprising culturing a somatic cell obtained from a transgenic [mammal] rat as claimed in claim 17 or 18 or ancestor thereof[according to the invention].

24. (Amended) A tissue derived from a somatic cell obtained from a transgenic [mammal] rat as claimed in claim 17 or 18 or ancestor thereof[according to the invention].

Please and add new claims 25-29 as follows:

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--25. A method of generating a cell line from a transgenic rat comprising a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to a cell specific promoter, the method comprising:

(i) maintaining the rat at restrictive conditions such that the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is expressed in vivo, only in a tissue of interest and in an inactive form such that the cells thereof grow normally;

(ii) culturing said cells from the tissue of interest in vitro under permissive conditions such that the immortalizing function is activated; and

(iii) subjecting the cells to non-permissive conditions so as to result in a cessation of growth and in differentiation.

26. A method as claimed in claim 25 wherein the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is a temperature sensitive gene.

27. A method as claimed in claim 25 or 26 wherein the permissive condition is a temperature of 33°C and the restrictive condition is a temperature of 39°C.

28. A method of testing a material suspected of being a carcinogen, said method comprising administering said material to a rat produced according to the method of claim 16 or an ancestor thereof and detecting neoplasms as an indication of carcinogenicity.

29. A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising administering said material to a rat produced according to the method of claim 16 or an ancestor thereof and detecting a reduced incidence of development of neoplasms, compared to an untreated rat, as an indication of said protection.--

REMARKS

Before amendment, claims 1-24 were pending. After amendment, claims 1, 3-4, 6-9, 13 and 15-29 are pending.

These amendments are supported throughout the present specification. No new matter is introduced by these amendments.